STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 164433

TO: Kevin Weddington **Location: rem/3a65/3c70** **Art Unit: 1614** **Wednesday, August 17, 2005** **Case Serial Number: 10/631029**	**From: Mary Hale** **Location: Biotech/Chem Library** **Rem 1D86** **Phone: 2-2507** **Mary.Hale@uspto.gov**

Search Notes

Feel free to contact me if you have any questions.

Note -- results are printed on both sides of printout

REM-3C70 ATTN: MITKY

ACCESS DB # 162711

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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: K. Weddington Examiner #: 68082 Date: 8-16-05
Art Unit: 1614 Phone Number: 2-0587 Serial Number: 10/634,029
Location (Bldg/Room#): REM-3A65 (Mailbox #): _____ Results Format Preferred (circle): (PAPER) DISK
****

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following: MEJ

Title of Invention: _____

Inventors (please provide full names): Rajinder Singh; Ankush Argade; Donald G. Payan; Holger Keim; Somasekhar Bhamidipati; Catherine Sylvain; Hui Li

Earliest Priority Date: _____

Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known.

For Sequence Searches Only ***Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***

Treating an autoimmune disease with a 2,4-pyrimidinediamine compound

the compounds are

R921302
R926891
R940323
R940347
R921303

The autoimmune disease is selected from

~~rheuma~~ rheumatoid arthritis
systemic lupus erythematosis
multiple sclerosis
autoimmune encephalomyelitis

****

STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: _____	____ NA Sequence (#)	____ STN ____ Dialog
Searcher Phone #: _____	____ AA Sequence (#)	____ Questel/Orbit ____ Lexis/Nexis
Searcher Location: _____	____ Structure (#)	____ Westlaw ____ WWW/Internet
Date Searcher Picked Up: _____	____ Bibliographic	____ In-house sequence systems
Date Completed: _____	____ Litigation	____ Commercial ____ Oligomer ____ Score/Length ____ Interference ____ SPDI ____ Encode/Transl
Searcher Prep & Review Time: _____	____ Fulltext	____ Other (specify)
Online Time: _____	____ Other	

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=> fil reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:15:38 ON 17 AUG 2005
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   16 AUG 2005  HIGHEST RN 860495-66-5
DICTIONARY FILE UPDATES:  16 AUG 2005  HIGHEST RN 860495-66-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
*********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e "2,4-pyrimidinediamine"/cn 5
E1            1     2,4-PYRIMIDINEDIACETONITRILE, 6-AMINO-5-CYANO-A2-(PHEN
                    YLMETHYLENE)-/CN
E2            1     2,4-PYRIMIDINEDIACETONITRILE, 6-AMINO-5-CYANO-A4-((3-C
                    YANO-4,5,6,7-TETRAHYDROBENZO(B)THIEN-2-YL)HYDRAZONO)-/CN
E3            1 --> 2,4-PYRIMIDINEDIAMINE/CN
E4            1     2,4-PYRIMIDINEDIAMINE, 1,2-DIHYDRO-N,N'-BIS(4-METHYLPHENYL)-
                    1-NITRO-/CN
E5            1     2,4-PYRIMIDINEDIAMINE, 1,4-DIHYDRO-N2,N2-DIMETHYL-, ION(1-)/
                    CN

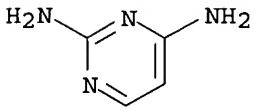
=> s e3;d ide can
L1            1 "2,4-PYRIMIDINEDIAMINE"/CN



L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   156-81-0  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   2,4-Pyrimidinediamine (9CI)  (CA INDEX NAME)


Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
```

OTHER CA INDEX NAMES:
CN Pyrimidine, 2,4-diamino- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 2,4-Diaminopyrimidine
CN NSC 30856
FS 3D CONCORD
DR 42910-88-3, 42910-89-4, 42910-90-7, 42910-92-9
MF C4 H6 N4
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, MEDLINE, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

254 REFERENCES IN FILE CA (1907 TO DATE)
44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
254 REFERENCES IN FILE CAPLUS (1907 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:138607

REFERENCE 2: 143:72294

REFERENCE 3: 142:254587

REFERENCE 4: 142:212327

REFERENCE 5: 142:74474

REFERENCE 6: 142:38288

REFERENCE 7: 141:260782

REFERENCE 8: 141:93976

REFERENCE 9: 141:76686

REFERENCE 10: 141:76353

=> e "r 921302"/cn 5
E1 1 R 91650/CN
E2 1 R 920K/CN
E3 0 --> R 921302/CN
E4 1 R 922/CN
E5 1 R 922-1/CN

=> e "r921302"/cn 5

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
E1            1     R9 STEEL/CN
E2            1     R900/CN
E3            0 --> R921302/CN
E4            1     R9F4K5/CN
E5            1     R9F5/CN

=> e "r 926891"/cn 5
E1            1     R 925SH3/CN
E2            1     R 92625/CN
E3            0 --> R 926891/CN
E4            1     R 9298/CN
E5            3     R 930/CN

=> e "r926891"/cn 5
E1            1     R9 STEEL/CN
E2            1     R900/CN
E3            0 --> R926891/CN
E4            1     R9F4K5/CN
E5            1     R9F5/CN

=> e "r 940323"/cn 5
E1            1     R 9403/CN
E2            1     R 9403, HOMOPOLYMER/CN
E3            0 --> R 940323/CN
E4            1     R 94138/CN
E5            1     R 9422/CN

=> e "r940323"/cn 5
E1            1     R9 STEEL/CN
E2            1     R900/CN
E3            0 --> R940323/CN
E4            1     R9F4K5/CN
E5            1     R9F5/CN

=> e "r 940347"/cn 5
E1            1     R 9403/CN
E2            1     R 9403, HOMOPOLYMER/CN
E3            0 --> R 940347/CN
E4            1     R 94138/CN
E5            1     R 9422/CN

=> e "r940347"/cn 5
E1            1     R9 STEEL/CN
E2            1     R900/CN
E3            0 --> R940347/CN
E4            1     R9F4K5/CN
E5            1     R9F5/CN

=> e "r 921303"/cn 5
E1            1     R 91650/CN
E2            1     R 920K/CN
E3            0 --> R 921303/CN
E4            1     R 922/CN
E5            1     R 922-1/CN

=> e "r921303"/cn 5
E1            1     R9 STEEL/CN
E2            1     R900/CN
E3            0 --> R921303/CN
E4            1     R9F4K5/CN
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
E5            1     R9F5/CN

=> fil medl,biosis,embase,caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         7.96       8.17

FILE 'MEDLINE' ENTERED AT 10:17:20 ON 17 AUG 2005

FILE 'BIOSIS' ENTERED AT 10:17:20 ON 17 AUG 2005
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FILE 'CAPLUS' ENTERED AT 10:17:20 ON 17 AUG 2005
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> s (autoimmune disease or autoimmune encephalomyelit? or rheumatoid arthrit? or
systemic lupus erythematos? or multiple sclerosis)
L2       136215 FILE MEDLINE
L3       119817 FILE BIOSIS
L4       136957 FILE EMBASE
L5        60193 FILE CAPLUS

TOTAL FOR ALL FILES
L6       453182 (AUTOIMMUNE DISEASE OR AUTOIMMUNE ENCEPHALOMYELIT? OR RHEUMATOID
                ARTHRIT? OR SYSTEMIC LUPUS ERYTHEMATOS? OR MULTIPLE SCLEROSIS)

=> s c20.111?
L7             0 FILE MEDLINE
L8             0 FILE BIOSIS
L9             0 FILE EMBASE
TERM '111?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED
You have entered a truncated stem which occurs in too many terms.
Make the stem longer and try again.  For example, if your original
term was 'degr?' to search for variations and the abbreviation for
'degradation', you could replace it with the expression '(degrdn OR
degrad?)'.  If your search term was numeric, e.g., 'C>5', reduce the
size of the range.

=> s c20.111?/ct
L10      250623 FILE MEDLINE
L11       50150 FILE BIOSIS
L12           0 FILE EMBASE
L13           0 FILE CAPLUS

TOTAL FOR ALL FILES
L14      300773 C20.111?/CT

=> s l1 or "2,4-pyrimidinediamine" or "2,4-diaminopyridine" or nsc 30856 or
r(w)(921302 or 926891 or 940323 or 940347 or 921303) or r921302 or r926891 or
r940323 or r940347 or r921303
L15          39 FILE MEDLINE
L16          62 FILE BIOSIS
L17          35 FILE EMBASE
L18         351 FILE CAPLUS
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TOTAL FOR ALL FILES
L19 487 L1 OR "2,4-PYRIMIDINEDIAMINE" OR "2,4-DIAMINOPYRIDINE" OR NSC 30856 OR R(W)(921302 OR 926891 OR 940323 OR 940347 OR 921303) OR R921302 OR R926891 OR R940323 OR R940347 OR R921303

=> s l19 and (l6 or l15)
L20 39 FILE MEDLINE
<------User Break------>

SEARCH ENDED BY USER

=> s l19 and (l6 or l14)
L22 0 FILE MEDLINE
L23 0 FILE BIOSIS
L24 1 FILE EMBASE
L25 12 FILE CAPLUS

TOTAL FOR ALL FILES
L26 13 L19 AND (L6 OR L14)

=> dup rem l26
PROCESSING COMPLETED FOR L26
L27 13 DUP REM L26 (0 DUPLICATES REMOVED)

=> d 1-13 ibib abs hitstr

L27 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:158647 CAPLUS
DOCUMENT NUMBER: 142:261547
TITLE: Preparation of **2,4-pyrimidinediamines** useful in the treatment of neoplastic diseases, inflammatory and immune system disorders
INVENTOR(S): Garcia-echeverria, Carlos; Kanazawa, Takanori; Kawahara, Eiji; Masuya, Keiichi; Matsuura, Naoko; Miyake, Takahiro; Ohmori, Osamu; Umemura, Ichiro; Steensma, Ruo; Chopiuk, Greg; Jiang, Jiqing; Wan, Yongqin; Ding, Qiang; Zhang, Qiong; Gray, Nathanael Schiander; Karanewsky, Donald
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.; IRM LLC
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016894	A1	20050224	WO 2004-EP9099	20040813

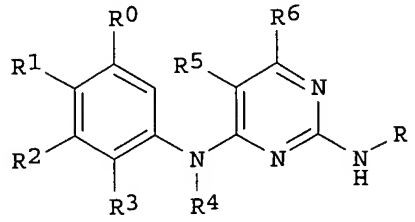
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-19227 A 20030815
GB 2003-22370 A 20030924

OTHER SOURCE(S): MARPAT 142:261547

GI



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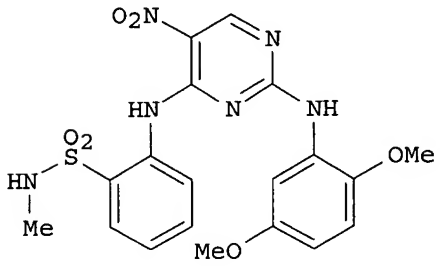


II

AB The title compds. I [R = aryl, heteroaryl, cycloalkyl and heterocycloalkyl; R0-R3 = H, alkyl, cycloalkyl, etc.; R4 = H, alkyl; R5, R6 = H, alkyl, alkoxyalkyl, etc.], useful for the manufacture of a medicament for the treatment or prevention of a disease which responds to inhibition of FAK and/or ALK and/or ZAP-70 and/or IGF-IR, were prepared and formulated. E.g., a 2-step synthesis of II, starting from 2,4-dichloro-5-nitropyrimidine and 2-amino-N-methylbenzenesulfonamide, was given. The compds. I have IC50 values in the range of 10 nM to 2 μM in cell-free ZAP-70 kinase assay.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:158646 CAPLUS
DOCUMENT NUMBER: 142:254587
TITLE: Methods for treating or preventing **autoimmune diseases** with **2,4-pyrimidinediamine** compounds
INVENTOR(S): Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati, Somasekhar; Carroll, David; Sylvain, Catherine; Clough, Jeffrey; Keim, Holger
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 276 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016893	A2	20050224	WO 2004-US24716	20040730
WO 2005016893	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-491641P P 20030730
US 2003-531598P P 20031219
US 2004-572246P P 20040518

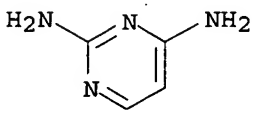
OTHER SOURCE(S): MARPAT 142:254587

AB The invention provides methods for treating or preventing **autoimmune diseases** with **2,4-pyrimidinediamine** compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of **autoimmune diseases** that can be treated or prevented with the compds. include **rheumatoid arthritis** and/or its associated symptoms, **systemic lupus erythematosis** and/or its associated symptoms and **multiple sclerosis** and/or its associated symptoms.

IT **156-81-0D, 2,4-Pyrimidinediamine,** derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidinediamine compds. for treatment or prevention of **autoimmune diseases**)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)



L27 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:120923 CAPLUS

DOCUMENT NUMBER: 142:219300

TITLE: **2,4-Pyrimidinediamines** for use in the treatment or prevention of **autoimmune diseases**

INVENTOR(S): Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati, Somasekhar; Carroll, David; Sylvain, Catherine; Clough, Jeffrey; Keim, Holger

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

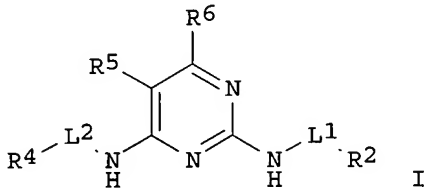
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012294	A1	20050210	WO 2004-US24920	20040730

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2003-491641P P 20030730
US 2003-531598P P 20031219
US 2004-572246P P 20040518

OTHER SOURCE(S): MARPAT 142:219300
GI



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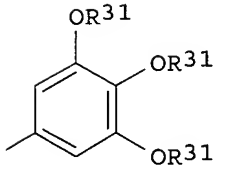
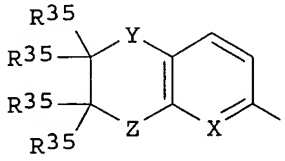


II



III

AB The present invention provides methods of treating or preventing **autoimmune diseases** with **2,4-pyrimidinediamine** compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl, alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un)substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of **autoimmune diseases** that can be treated or prevented with the compds. I include **rheumatoid arthritis** and/or its associated symptoms, **systemic lupus erythematosus** and/or its associated symptoms and **multiple sclerosis** and/or its associated symptoms. The general procedures for synthesis of compds. I are described. The characterization data for over 500 prepared

compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5-fluoro-N2-(3,4,5-trimethoxyphenyl)-**2,4-pyrimidinediamine** showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

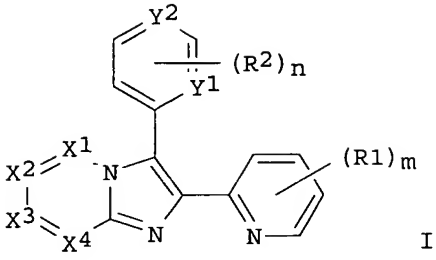
L27 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:220155 CAPLUS
DOCUMENT NUMBER: 140:270866
TITLE: Preparation of (pyridinyl)(pyrimidinyl)imidazo[1,2-a]pyridines as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors
INVENTOR(S): Lee, Wen-cherng; Carter, Mary Beth; Sun, Lihong; Chuaqui, Claudio; Singh, Juswinder; Boriack-Sjodin, Paula; Choi, Michael S.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004021989	A2	20040318	WO 2003-US27721	20030905
WO 2004021989	A3	20040923		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2497968	AA	20040318	CA 2003-2497968	20030905
EP 1546112	A2	20050629	EP 2003-752004	20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014052	A	20050705	BR 2003-14052	20030905

PRIORITY APPLN. INFO.: US 2002-408812P P 20020906
WO 2003-US27721 W 20030905

OTHER SOURCE(S): MARPAT 140:270866
GI



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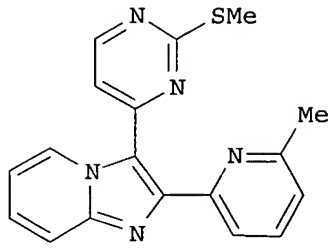
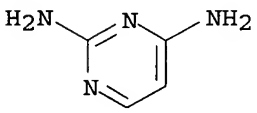


II

AB Title compds. I [wherein X1, X2, X3, X4 = independently CRx or N, only two of them can be N simultaneously; Y1, Y2 = independently CRa or N, at least one of them must be N; R1 = independently alkyl, alkenyl, alkynyl, alkoxy, acyl, urea, cycloalkylsulfanyl, etc.; R2 = independently alkyl, alkenyl, alkynyl, acyl, halo, -N(alkyl)(cycloalkyl), heteroaroyl, etc.; m = 0-4; n = 0-3; Rx, Ra = independently hydrogen, alkyl, alkenyl, hydroxy, guanidino, amidino, cycloalkylcarbonylamino, etc.; and pharmaceutically acceptable salts or N-oxides thereof] were prepared as antagonists against transforming growth factor β (TGFβ) family type I receptors, Alk5 and Alk4. For example, methylation of 2-mercapto-4-methylpyrimidine with MeI, followed by reaction with 6-methylpyridine-2-carboxylic acid Et ester and cyclocondensation with 2-aminopyridine, gave II. I exhibited TGFβ-induced PAI-Luciferase reporter activity with IC50 values of less than 10μM and cytotoxicity with LD25 values greater than 10μM. Thus, I and their pharmaceutical compns. are useful as antagonists for preventing and/or treating numerous diseases, including fibrotic disorders and tumors.

IT **156-81-0**, 2,4-Diaminopyrimidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (pyridinyl)(pyrimidinyl)imidazo[1,2-a]pyridines as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors)

RN 156-81-0 CAPLUS
CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)



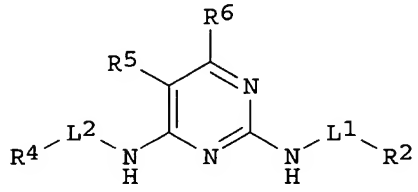
L27 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:142963 CAPLUS
DOCUMENT NUMBER: 140:199334
TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or IgG receptor modulators for treatment of autoimmune diseases
INVENTOR(S): Singh, Rajinder; Argade, Ankush; Payan, Donald G.; Clough, Jeffrey; Keim, Holger; Sylvain, Catherine; Li, Hui; Bhamidipati, Somasekhar
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, USA
SOURCE: PCT Int. Appl., 811 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004014382	A1	20040219	WO 2003-US24087		20030729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2492325	AA	20040219	CA 2003-2492325		20030729
EP 1534286	A1	20050601	EP 2003-784871		20030729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003013059	A	20050705	BR 2003-13059		20030729
US 2005038243	A1	20050217	US 2004-858343		20040601
SE 2005000203	A	20050329	SE 2005-203		20050127
PRIORITY APPLN. INFO.:			US 2002-399673P	P	20020729
			US 2003-443949P	P	20030131
			US 2003-452339P	P	20030306
			US 2003-631029	A	20030729
			US 2002-353267P	P	20020201
			US 2002-353333P	P	20020201
			US 2002-434277P	P	20021217
			US 2003-355543	A1	20030131
			WO 2003-US24087	W	20030729

OTHER SOURCE(S): MARPAT 140:199334
GI



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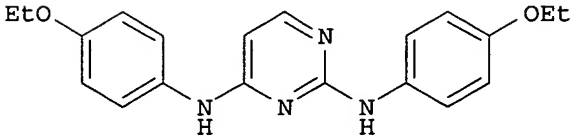

II

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a

linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4-pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM, resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20322 CAPLUS
DOCUMENT NUMBER: 140:87658
TITLE: Peptidomimetic modulators of cell adhesion
INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni, Feng; Chen, Zhigang; Michaud, Stephanie Denise; Wang, Shaomeng; Hu, Zengjian
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 280 pp., Cont.-in-part of U.S. Ser. No. 6,982.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004006011	A1	20040108	US 2003-425557	20030428
US 6031072	A	20000229	US 1997-893534	19970711
US 6326352	B1	20011204	US 2000-507102	20000217
US 2002168761	A1	20021114	US 2001-769145	20010124
US 2002151475	A1	20021017	US 2001-6982	20011204
US 6914044	B2	20050705		

PRIORITY APPLN. INFO.:

US 1996-21612P	P	19960712
US 1997-893534	A1	19970711
US 2000-491078	B2	20000124
US 2000-507102	A1	20000217
US 2001-769145	B2	20010124
US 2001-6982	A2	20011204

OTHER SOURCE(S): MARPAT 140:87658
AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such

peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

L27 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:737756 CAPLUS
DOCUMENT NUMBER: 139:261319
TITLE: Preparation of 5-bromo-**2,4**-**pyrimidinediamines** and related compounds as cyclin dependent kinase inhibitors
INVENTOR(S): Luecking, Ulrich; Krueger, Martin; Jautelat, Rolf; Prien, Olaf; Siemeister, Gerd; Ernst, Alexander
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003076437	A1	20030918	WO 2003-EP1995		20030226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
DE 10212100	A1	20031023	DE 2002-10212100		20020311
DE 10255984	A1	20040812	DE 2002-10255984		20021126
EP 1483260	A1	20041208	EP 2003-708151		20030226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2004063737	A1	20040401	US 2003-384787		20031027
PRIORITY APPLN. INFO.:			DE 2002-10212100	A	20020311
			DE 2002-10255984	A	20021126
			US 2002-363878P	P	20020314
			US 2002-430053P	P	20021202
			WO 2003-EP1995	W	20030226

OTHER SOURCE(S): MARPAT 139:261319
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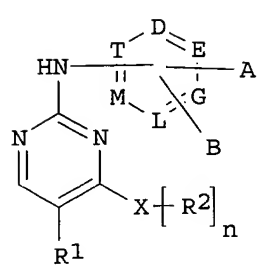

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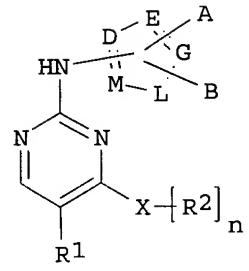

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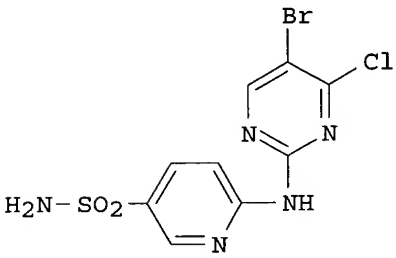

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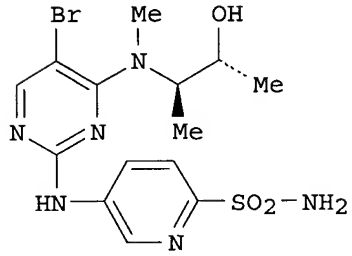


IV

AB Title compds. I and II [D, E, G, L, M, T = C, O, N, S atom whereby at least a heteroatom must be contained in the ring; R1 = H, halo, alkyl, etc.; R2 = H, alkyl, alkenyl, etc.; A, B = H, OH, halo, etc.; n = 0, 1 with provisos] and their pharmaceutically acceptable salts were prepared For example, condensation of chloropyrimidine III, e.g., prepared from 5-bromo-2-chloro-4-hydroxypyrimidine in 2-steps, and threo-3-methylaminobutan-2-ol afforded pyrimidinediamine IV in 75% yield. In CDK2/CycE inhibition studies, 24-examples of compds. I exhibited IC50 values ranging from 6-74 nM. Compds. I are claimed useful as cardiovascular, antiviral, antitumor, etc. agents.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:133036 CAPLUS
DOCUMENT NUMBER: 138:180679
TITLE: SH3 protein domains and their ligands
INVENTOR(S): Booker, Grant William; Pyke, Simon Mathew; Branson, Kim Mathew; Inglis, Steven Robert
PATENT ASSIGNEE(S): Adelaide Research & Innovation Pty Ltd., Australia
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013523	A1	20030220	WO 2002-AU1064	20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2001-6881 A 20010808
OTHER SOURCE(S): MARPAT 138:180679

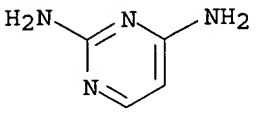
AB The present invention relates generally to mols. capable of interaction with one or more domains within a proteinaceous mol. such as a peptide, polypeptide, protein or a macromol. comprising a proteinaceous mol. More particularly the present invention relates to mols. including ligands which are capable of interacting with, and more particularly, binding to, SH3 protein domains or homologs thereof and even more particularly to mols. including ligands which are capable of binding to SH3 domains having a three-dimensional ligand-binding site comprising a neg. charged residue and a hydrophobic residue linearly separated by at least five amino acid residues. The subject invention is preferably directed to the use of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and derivs., homologs, analogs and mimetics thereof or pharmaceutically acceptable salts thereof which interact with SH3 domains, and more particularly to the binding of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and derivs. analogs and mimetics to SH3 domains as defined above. The present invention contemplates the use of a three dimensional structure of the subject SH3 domain to identify, screen and design amino-substituted and amino-substituted pyridines and aminoquinolines capable of binding to an SH3 domain. The present invention is also useful for the in silico selection of derivs. homologs, analogs and mimetics of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline capable of binding to SH3 domains. The ligands of the present invention are useful in the development of a range of therapeutic and diagnostic agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:91269 CAPLUS
DOCUMENT NUMBER: 139:62596
TITLE: Imidazopyrimidines, potent inhibitors of p38 MAP kinase
AUTHOR(S): Rupert, Kenneth C.; Henry, James R.; Dodd, John H.; Wadsworth, Scott A.; Cavender, Druie E.; Olini, Gilbert C.; Fahmy, Bohumila; Siekierka, John J.
CORPORATE SOURCE: L.L.C., Drug Discovery, Johnson & Johnson Pharmaceutical Research and Development, Raritan, NJ, 08869, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(3), 347-350
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:62596

AB The MAP kinase p38 is implicated in the release of the pro-inflammatory cytokines TNF-α and IL-1β. Inhibition of cytokine release may be a useful treatment for inflammatory conditions such as **rheumatoid arthritis** and Crohn's disease. A novel series of imidazopyrimidines have been discovered that potently inhibit p38 and suppress the production of TNF-α in vivo.

IT **156-81-0, 2,4-Pyrimidinediamine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(imidazopyrimidines, potent inhibitors of p38 MAP kinase)
RN 156-81-0 CAPLUS
CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:449449 CAPLUS
DOCUMENT NUMBER: 137:33318
TITLE: Preparation of pyrimidinylaminothiazoles as tyrosine kinase inhibitors.
INVENTOR(S): Bilodeau, Mark T.; Hartman, George D.; Hoffman, Jacob M., Jr.; Lumma, William C., Jr.; Manley, Peter J.; Rodman, Leonard; Sisko, John T.; Smith, Anthony M.; Tucker, Thomas J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002045652	A2	20020613	WO 2001-US44573	20011130
WO 2002045652	A3	20020822		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002137755	A1	20020926	US 2001-990473	20011121
CA 2429728	AA	20020613	CA 2001-2429728	20011130
AU 2002032441	A5	20020618	AU 2002-32441	20011130
EP 1341540	A2	20030910	EP 2001-991965	20011130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004524282	T2	20040812	JP 2002-547438	20011130
US 2004063720	A1	20040401	US 2003-677687	20031002

PRIORITY APPLN. INFO.:		
US 2000-251006P	P	20001204
US 2001-990473	A1	20011121
WO 2001-US44573	W	20011130

OTHER SOURCE(S): MARPAT 137:33318
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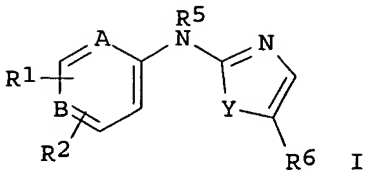


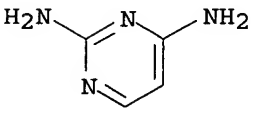
I

AB Title compds. [I; A, B = N, NO; Y = O, S, NR4; R1, R2 = H, perfluoroalkoxy, OH, cyano, halo, (substituted) alkyl(oxy)(carbonyl), aryl(oxy)(carbonyl), heterocyclyl, etc.; R4 = H, aryl, alkyl; R5 = H, SO2Rc, CORc, Rc, CO2Rc; R6 = aryl, cyano, halo, (substituted) alkyl, alkenyl, alkynyl, heterocyclyl, aminocarbonyl; Rc = alkyl, aryl, heterocyclyl], were prepared for treating angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammation, etc. Thus, 4-aminopyrimidine was stirred with NaH in THF; 2-bromo-5-phenylthiazole was added and the mixture was refluxed overnight to give 5-phenylthiazol-2-yl pyrimidin-4-yl amine. I inhibited vascular endothelial growth factor-stimulated mitogenesis of human vascular endothelial cells with IC50 = 0.01-5.0 nM.

IT **156-81-0**, 2,4-Diaminopyrimidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimidinylaminothiazoles as tyrosine kinase inhibitors)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)



L27 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:869496 CAPLUS

DOCUMENT NUMBER: 137:363033

TITLE: Peptidomimetic modulators of cell adhesion

INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni, Feng; Chen, Zhigang; Michaud, Stephanie D.; Wang, Shoameng; Hu, Zenjian

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 309 pp., Cont.-in-part of U.S. Ser. No. 491,078.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002168761	A1	20021114	US 2001-769145	20010124
US 2004058864	A1	20040325	US 2003-412701	20030410
US 2004006011	A1	20040108	US 2003-425557	20030428
PRIORITY APPLN. INFO.:			US 2000-491078	A2 20000124
			US 1996-21612P	P 19960712
			US 1997-893534	A1 19970711

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

	US 2000-507102	A1 20000217
	US 2001-769145	B1 20010124
	US 2001-6982	A2 20011204

OTHER SOURCE(S): MARPAT 137:363033

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

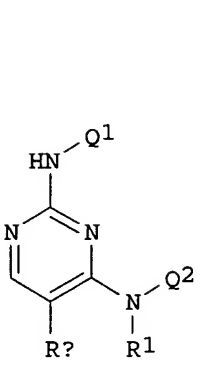
L27 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:457043 CAPLUS
DOCUMENT NUMBER: 133:89537
TITLE: Preparation of **2,4-pyrimidinediamine** derivatives as anticancer agents
INVENTOR(S): Bradbury, Robert Hugh; Breault, Gloria Anne; Jewsbury, Philip John; Pease, Janet Elizabeth
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039101	A1	20000706	WO 1999-GB4325	19991220
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2352896	AA	20000706	CA 1999-2352896	19991220
EP 1140860	A1	20011010	EP 1999-962375	19991220
EP 1140860	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916590	A	20011023	BR 1999-16590	19991220
JP 2002533446	T2	20021008	JP 2000-591012	19991220
AU 763091	B2	20030710	AU 2000-18743	19991220
NZ 512118	A	20030829	NZ 1999-512118	19991220
AT 277020	E	20041015	AT 1999-962375	19991220
ES 2228145	T3	20050401	ES 1999-962375	19991220
ZA 2001004413	A	20020829	ZA 2001-4413	20010529
NO 2001003038	A	20010822	NO 2001-3038	20010619
US 6593326	B1	20030715	US 2001-868602	20010823

PRIORITY APPLN. INFO.:		GB 1998-28511	A 19981224
		WO 1999-GB4325	W 19991220

OTHER SOURCE(S): MARPAT 133:89537
GI



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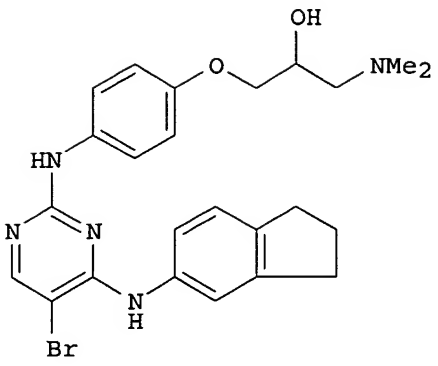

II

AB The present invention relates to the title compds. (I) [wherein R1 = H, (un)substituted alkyl, alkenyl, or alkynyl, benzyl, 2-phenylethyl, phthalimidoalkyl, or cycloalkylalkyl; Rx = halo, OH, NO2, NH2, CN, SH, CO2H, SO2NH2, NHCHO, ureido, etc.; Q1 and Q2 = independently (un)substituted aryl, 5- or 6-membered monocycle, or 9- or 10-membered bicyclic heterocycle], processes for their manufacture, and pharmaceutical compns. containing them. For example, addition of 4-[2-hydroxy-3-(N,N-dimethylamino)propoxy]aniline•HCl in MeOH to 5-bromo-2-chloro-4-(indan-5-ylamino)pyrimidine in BuOH (prepns. given) and heating to 100°C for 18 h gave II (42%). I inhibited the effects of cylin-dependent serine/threonine kinases (CDKs), showing selectivity for CDK2 (no data), CDK4 (IC50 ranging from 0.02 μM to 0.07 μM), and CDK6 (no data). In a tyrosine kinase activity assay using Sf21 cells transfected with plaque-pure FAK recombinant virus, I also inhibited focal adhesion kinase 3 (FAK3) with IC50 ranging from 0.032 μM to 0.07 μM. Typical IC50 values for I when tested for inhibition of cell growth in an Sulforhodamine B (SRB) assay were in the range of 1 mM to 1 nM. Thus, I possess anti-cancer properties, including anti-cell-migration, antiproliferation and/or apoptotic properties. Such properties are expected to be of value in the treatment of disease states associated with aberrant cell cycles and cell proliferation such as cancers (solid tumors and leukemias), fibroproliferative and differentiative disorders, psoriasis, **rheumatoid arthritis**, Kaposi's sarcoma, hemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, **autoimmune diseases**, acute and chronic inflammation, bone diseases, and ocular diseases with retinal vessel proliferation.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 13 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 91081327 EMBASE
DOCUMENT NUMBER: 1991081327
TITLE: Therapy of acute and chronic **multiple sclerosis.**
AUTHOR: Tindall R.S.A.
CORPORATE SOURCE: Department of Neurology, University of Southern California, Los Angeles Veterans Administration Facility, 425 South Hill Street, Los Angeles, CA 90013, United States
SOURCE: Comprehensive Therapy, (1991) Vol. 17, No. 1, pp. 18-25. ISSN: 0098-8243 CODEN: COTHD3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

```
FILE SEGMENT:        008     Neurology and Neurosurgery
                     026     Immunology, Serology and Transplantation
                     037     Drug Literature Index
LANGUAGE:            English
ENTRY DATE:          Entered STN: 911216
                     Last Updated on STN: 911216
       DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER


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L28        2983 FILE MEDLINE
L29        7931 FILE BIOSIS
L30        2556 FILE EMBASE
L31        9987 FILE CAPLUS

TOTAL FOR ALL FILES
L32       23457 SINGH R?/AU


L33           1 FILE MEDLINE
L34           8 FILE BIOSIS
L35           7 FILE EMBASE
L36          21 FILE CAPLUS

TOTAL FOR ALL FILES
L37          37 ARGADE A?/AU


L38         144 FILE MEDLINE
L39         206 FILE BIOSIS
L40         138 FILE EMBASE
L41         158 FILE CAPLUS

TOTAL FOR ALL FILES
L42         646 PAYAN D?/AU

=> s l32 and l37 and l42
L43           0 FILE MEDLINE
L44           1 FILE BIOSIS
L45           0 FILE EMBASE
L46           2 FILE CAPLUS

TOTAL FOR ALL FILES
L47           3 L32 AND L37 AND L42

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L48           0 FILE MEDLINE
L49           1 FILE BIOSIS
L50           0 FILE EMBASE
L51           1 FILE CAPLUS

TOTAL FOR ALL FILES
L52           2 L47 NOT L26

=> dup rem l52
PROCESSING COMPLETED FOR L52
L53            2 DUP REM L52 (0 DUPLICATES REMOVED)

=> d ibib abs 1-2


Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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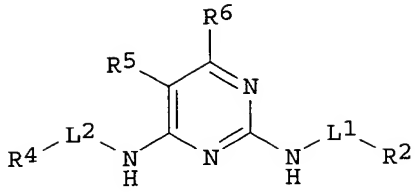
L53 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:610204 CAPLUS
DOCUMENT NUMBER: 139:164801
TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or IgG receptor modulators for treatment of allergic diseases, inflammatory conditions, and tissue destruction
INVENTOR(S): **Singh, Rajinder**; **Argade, Ankush**; **Payan, Donald G.**; Molineaux, Susan; Holland, Sacha J.; Clough, Jeffrey; Keim, Holger; Bhamidipati, Somasekhar; Sylvain, Catherine; Li, Weigun; Rossi, Alexander B.
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 648 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003063794	A2	20030807	WO 2003-US3022		20030131
WO 2003063794	A3	20031204			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2474277	AA	20030807	CA 2003-2474277		20030131
US 2004029902	A1	20040212	US 2003-355543		20030131
EP 1471915	A2	20041103	EP 2003-707654		20030131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005516046	T2	20050602	JP 2003-563490		20030131
US 2005038243	A1	20050217	US 2004-858343		20040601
PRIORITY APPLN. INFO.:			US 2002-353267P	P	20020201
			US 2002-353333P	P	20020201
			US 2002-399673P	P	20020729
			US 2002-434277P	P	20021217
			US 2003-355543	A1	20030131
			WO 2003-US3022	W	20030131

OTHER SOURCE(S): MARPAT 139:164801
GI



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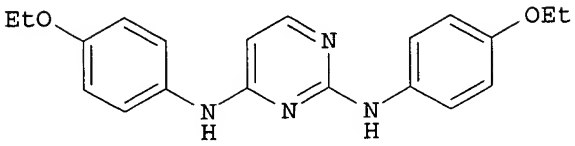

II

AB Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4-pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM, resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. The treatment and prevention of allergic diseases, low grade scarring, diseases associated with tissue destruction, diseases associated with tissue inflammation, inflammation, and scarring are targeted uses (no data).

L53 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:165568 BIOSIS
DOCUMENT NUMBER: PREV200200165568
TITLE: Development and utilization of cultured human mast cells for high throughput small molecule drug discovery.
AUTHOR(S): Rossi, Alexander [Reprint author]; Holland, Sacha [Reprint author]; Woronicz, John [Reprint author]; Quast, Jeff [Reprint author]; **Argade, Ankush**; Sylvain, Catherine; Juencke, Sara; Sula, Caroline; Tombo, Wendy [Reprint author]; Goodrich, Bethany; Pine, Polly; Scheerens, Heleen; Natarajan, Gita; Li, Wenbao; Bennett, Mark [Reprint author]; Daniel, Ruby; Wagner, Gregory; **Singh, Rajinder**; Molineaux, Susan [Reprint author]; **Payan, Donald**
CORPORATE SOURCE: Cell Biology, Rigel Pharmaceuticals, Inc., 240 East Grand Avenue, So. San Francisco, CA, 94080, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 512a-513a. print.
Meeting Info.: 41st Annual Meeting of the American Society

for Cell Biology. Washington DC, USA. December 08-12, 2001.
American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002

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L54          84 FILE MEDLINE
L55          57 FILE BIOSIS
L56          57 FILE EMBASE
L57          70 FILE CAPLUS

TOTAL FOR ALL FILES
L58         268 KEIM H?/AU


L59           8 FILE MEDLINE
L60          18 FILE BIOSIS
L61           7 FILE EMBASE
L62          16 FILE CAPLUS

TOTAL FOR ALL FILES
L63          49 BHAMIDIPATI S?/AU


L64           8 FILE MEDLINE
L65          13 FILE BIOSIS
L66          11 FILE EMBASE
L67          10 FILE CAPLUS

TOTAL FOR ALL FILES
L68          42 SYLVAIN C?/AU


L69        5342 FILE MEDLINE
L70        6316 FILE BIOSIS
L71        4069 FILE EMBASE
L72       21181 FILE CAPLUS

TOTAL FOR ALL FILES
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L75           0 FILE BIOSIS
L76           0 FILE EMBASE
L77           3 FILE CAPLUS

TOTAL FOR ALL FILES
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=> s l78 not l52
L79           0 FILE MEDLINE
L80           0 FILE BIOSIS
L81           0 FILE EMBASE
L82           3 FILE CAPLUS
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TOTAL FOR ALL FILES
L83 3 L78 NOT L52

=> d 1-3 ibib abs

L83 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:158646 CAPLUS
DOCUMENT NUMBER: 142:254587
TITLE: Methods for treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compounds
INVENTOR(S): Rajinder, Singh; Ankush, Argade; **Li, Hui**; **Bhamidipati, Somasekhar**; Carroll, David; **Sylvain, Catherine**; Clough, Jeffrey; **Keim, Holger**
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 276 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016893	A2	20050224	WO 2004-US24716	20040730
WO 2005016893	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-491641P P 20030730
US 2003-531598P P 20031219
US 2004-572246P P 20040518
OTHER SOURCE(S): MARPAT 142:254587
AB The invention provides methods for treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosis and/or its associated symptoms and multiple sclerosis and/or its associated symptoms.

L83 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:120923 CAPLUS
DOCUMENT NUMBER: 142:219300
TITLE: 2,4-Pyrimidinediamines for use in the treatment or prevention of autoimmune diseases
INVENTOR(S): Rajinder, Singh; Ankush, Argade; **Li, Hui**; **Bhamidipati, Somasekhar**; Carroll, David; **Sylvain, Catherine**; Clough, Jeffrey; **Keim, Holger**
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

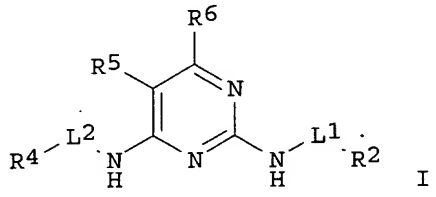
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012294	A1	20050210	WO 2004-US24920	20040730

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-491641P P 20030730
US 2003-531598P P 20031219
US 2004-572246P P 20040518

OTHER SOURCE(S): MARPAT 142:219300
GI



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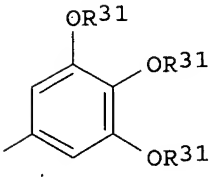
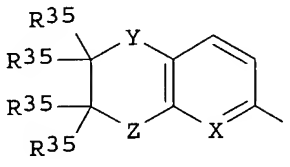


II



III

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl, alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un)substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. I include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosus and/or its associated symptoms and multiple sclerosis and/or its associated symptoms. The general procedures

for synthesis of compds. I are described. The characterization data for over 500 prepared compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5-fluoro-N2-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

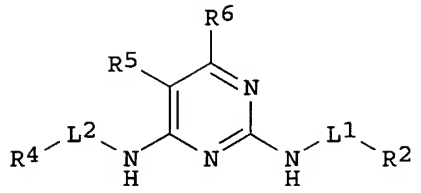
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:142963 CAPLUS
DOCUMENT NUMBER: 140:199334
TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or IgG receptor modulators for treatment of autoimmune diseases
INVENTOR(S): Singh, Rajinder; Argade, Ankush; Payan, Donald G.; Clough, Jeffrey; **Keim, Holger**; **Sylvain, Catherine**; **Li, Hui**; **Bhamidipati, Somasekhar**
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, USA
SOURCE: PCT Int. Appl., 811 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014382	A1	20040219	WO 2003-US24087	20030729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492325	AA	20040219	CA 2003-2492325	20030729
EP 1534286	A1	20050601	EP 2003-784871	20030729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013059	A	20050705	BR 2003-13059	20030729
US 2005038243	A1	20050217	US 2004-858343	20040601
SE 2005000203	A	20050329	SE 2005-203	20050127

PRIORITY APPLN. INFO.:		
US 2002-399673P	P	20020729
US 2003-443949P	P	20030131
US 2003-452339P	P	20030306
US 2003-631029	A	20030729
US 2002-353267P	P	20020201
US 2002-353333P	P	20020201
US 2002-434277P	P	20021217
US 2003-355543	A1	20030131
WO 2003-US24087	W	20030729

OTHER SOURCE(S): MARPAT 140:199334
GI



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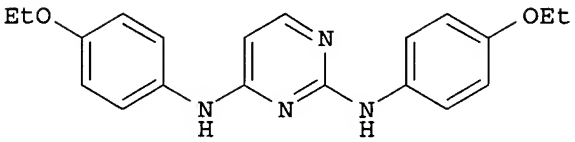

II

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4-pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM, resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his

(FILE 'HOME' ENTERED AT 10:15:21 ON 17 AUG 2005)

FILE 'REGISTRY' ENTERED AT 10:15:38 ON 17 AUG 2005
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L1 1 S E3
E "R 921302"/CN 5
E "R921302"/CN 5
E "R 926891"/CN 5

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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                E "R926891"/CN 5
                E "R 940323"/CN 5
                E "R940323"/CN 5
                E "R 940347"/CN 5
                E "R940347"/CN 5
                E "R 921303"/CN 5
                E "R921303"/CN 5

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L3       119817 FILE BIOSIS
L4       136957 FILE EMBASE
L5        60193 FILE CAPLUS
     TOTAL FOR ALL FILES
L6       453182 S (AUTOIMMUNE DISEASE OR AUTOIMMUNE ENCEPHALOMYELIT? OR RHEUMAT
L7            0 FILE MEDLINE
L8            0 FILE BIOSIS
L9            0 FILE EMBASE
L10      250623 FILE MEDLINE
L11       50150 FILE BIOSIS
L12           0 FILE EMBASE
L13           0 FILE CAPLUS
     TOTAL FOR ALL FILES
L14      300773 S C20.111?/CT
L15          39 FILE MEDLINE
L16          62 FILE BIOSIS
L17          35 FILE EMBASE
L18         351 FILE CAPLUS
     TOTAL FOR ALL FILES
L19         487 S L1 OR "2,4-PYRIMIDINEDIAMINE" OR "2,4-DIAMINOPYRIDINE" OR NSC
L20          39 FILE MEDLINE
L21          62 FILE BIOSIS
L22           0 FILE MEDLINE
L23           0 FILE BIOSIS
L24           1 FILE EMBASE
L25          12 FILE CAPLUS
     TOTAL FOR ALL FILES
L26          13 S L19 AND (L6 OR L14)
L27          13 DUP REM L26 (0 DUPLICATES REMOVED)
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L29        7931 FILE BIOSIS
L30        2556 FILE EMBASE
L31        9987 FILE CAPLUS
     TOTAL FOR ALL FILES
L32       23457 S SINGH R?/AU
L33           1 FILE MEDLINE
L34           8 FILE BIOSIS
L35           7 FILE EMBASE
L36          21 FILE CAPLUS
     TOTAL FOR ALL FILES
L37          37 S ARGADE A?/AU
L38         144 FILE MEDLINE
L39         206 FILE BIOSIS
L40         138 FILE EMBASE
L41         158 FILE CAPLUS
     TOTAL FOR ALL FILES
L42         646 S PAYAN D?/AU
L43           0 FILE MEDLINE
L44           1 FILE BIOSIS
L45           0 FILE EMBASE
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L46             2 FILE CAPLUS
     TOTAL FOR ALL FILES
L47             3 S L32 AND L37 AND L42
L48             0 FILE MEDLINE
L49             1 FILE BIOSIS
L50             0 FILE EMBASE
L51             1 FILE CAPLUS
     TOTAL FOR ALL FILES
L52             2 S L47 NOT L26
L53             2 DUP REM L52 (0 DUPLICATES REMOVED)
L54            84 FILE MEDLINE
L55            57 FILE BIOSIS
L56            57 FILE EMBASE
L57            70 FILE CAPLUS
     TOTAL FOR ALL FILES
L58           268 S KEIM H?/AU
L59             8 FILE MEDLINE
L60            18 FILE BIOSIS
L61             7 FILE EMBASE
L62            16 FILE CAPLUS
     TOTAL FOR ALL FILES
L63            49 S BHAMIDIPATI S?/AU
L64             8 FILE MEDLINE
L65            13 FILE BIOSIS
L66            11 FILE EMBASE
L67            10 FILE CAPLUS
     TOTAL FOR ALL FILES
L68            42 S SYLVAIN C?/AU
L69          5342 FILE MEDLINE
L70          6316 FILE BIOSIS
L71          4069 FILE EMBASE
L72         21181 FILE CAPLUS
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L73         36908 S LI H?/AU
L74             0 FILE MEDLINE
L75             0 FILE BIOSIS
L76             0 FILE EMBASE
L77             3 FILE CAPLUS
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L78             3 S L58 AND L63 AND L68 AND L73
L79             0 FILE MEDLINE
L80             0 FILE BIOSIS
L81             0 FILE EMBASE
L82             3 FILE CAPLUS
     TOTAL FOR ALL FILES
L83             3 S L78 NOT L52

=> log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             138.76     146.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                             -11.68     -11.68

STN INTERNATIONAL LOGOFF AT 10:26:10 ON 17 AUG 2005
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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=> fil reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:15:38 ON 17 AUG 2005
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   16 AUG 2005  HIGHEST RN 860495-66-5
DICTIONARY FILE UPDATES:  16 AUG 2005  HIGHEST RN 860495-66-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e "2,4-pyrimidinediamine"/cn 5
E1            1      2,4-PYRIMIDINEDIACETONITRILE, 6-AMINO-5-CYANO-A2-(PHEN
                     YLMETHYLENE)-/CN
E2            1      2,4-PYRIMIDINEDIACETONITRILE, 6-AMINO-5-CYANO-A4-((3-C
                     YANO-4,5,6,7-TETRAHYDROBENZO(B)THIEN-2-YL)HYDRAZONO)-/CN
E3            1 --> 2,4-PYRIMIDINEDIAMINE/CN
E4            1      2,4-PYRIMIDINEDIAMINE, 1,2-DIHYDRO-N,N'-BIS(4-METHYLPHENYL)-
                     1-NITRO-/CN
E5            1      2,4-PYRIMIDINEDIAMINE, 1,4-DIHYDRO-N2,N2-DIMETHYL-, ION(1-)/
                     CN

=> s e3;d ide can
L1            1 "2,4-PYRIMIDINEDIAMINE"/CN



L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   156-81-0  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   2,4-Pyrimidinediamine (9CI)  (CA INDEX NAME)


Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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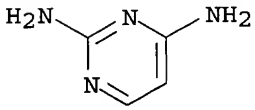
OTHER CA INDEX NAMES:
CN Pyrimidine, 2,4-diamino- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 2,4-Diaminopyrimidine
CN NSC 30856
FS 3D CONCORD
DR 42910-88-3, 42910-89-4, 42910-90-7, 42910-92-9
MF C4 H6 N4
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, MEDLINE, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

254 REFERENCES IN FILE CA (1907 TO DATE)
44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
254 REFERENCES IN FILE CAPLUS (1907 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:138607

REFERENCE 2: 143:72294

REFERENCE 3: 142:254587

REFERENCE 4: 142:212327

REFERENCE 5: 142:74474

REFERENCE 6: 142:38288

REFERENCE 7: 141:260782

REFERENCE 8: 141:93976

REFERENCE 9: 141:76686

REFERENCE 10: 141:76353

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E3 0 --> R 921302/CN
E4 1 R 922/CN
E5 1 R 922-1/CN

=> e "r921302"/cn 5

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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E1            1     R9 STEEL/CN
E2            1     R900/CN
E3            0 --> R921302/CN
E4            1     R9F4K5/CN
E5            1     R9F5/CN

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E4            1     R9F4K5/CN
E5            1     R9F5/CN

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E2            1     R 9403, HOMOPOLYMER/CN
E3            0 --> R 940323/CN
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E5            1     R9F5/CN

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E4            1     R 94138/CN
E5            1     R 9422/CN

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E5            1     R9F5/CN

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E2            1     R900/CN
E3            0 --> R921303/CN
E4            1     R9F4K5/CN
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       7.96       8.17

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FILE 'BIOSIS' ENTERED AT 10:17:20 ON 17 AUG 2005
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=> s (autoimmune disease or autoimmune encephalomyelit? or rheumatoid arthrit? or
systemic lupus erythematos? or multiple sclerosis)
L2       136215 FILE MEDLINE
L3       119817 FILE BIOSIS
L4       136957 FILE EMBASE
L5        60193 FILE CAPLUS

TOTAL FOR ALL FILES
L6       453182 (AUTOIMMUNE DISEASE OR AUTOIMMUNE ENCEPHALOMYELIT? OR RHEUMATOID
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You have entered a truncated stem which occurs in too many terms.
Make the stem longer and try again.  For example, if your original
term was 'degr?' to search for variations and the abbreviation for
'degradation', you could replace it with the expression '(degrdn OR
degrad?)'.  If your search term was numeric, e.g., 'C>5', reduce the
size of the range.

=> s c20.111?/ct
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L12           0 FILE EMBASE
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TOTAL FOR ALL FILES
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r(w)(921302 or 926891 or 940323 or 940347 or 921303) or r921302 or r926891 or
r940323 or r940347 or r921303
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L16          62 FILE BIOSIS
L17          35 FILE EMBASE
L18         351 FILE CAPLUS
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SEARCH ENDED BY USER

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L23          0 FILE BIOSIS
L24          1 FILE EMBASE
L25         12 FILE CAPLUS

TOTAL FOR ALL FILES
L26         13 L19 AND (L6 OR L14)

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PROCESSING COMPLETED FOR L26
L27          13 DUP REM L26 (0 DUPLICATES REMOVED)

=> d 1-13 ibib abs hitstr

L27  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:158647  CAPLUS
DOCUMENT NUMBER:          142:261547
TITLE:                    Preparation of 2,4-
                          pyrimidinediamines useful in the treatment of
                          neoplastic diseases, inflammatory and immune system
                          disorders
INVENTOR(S):              Garcia-echeverria, Carlos; Kanazawa, Takanori;
                          Kawahara, Eiji; Masuya, Keiichi; Matsuura, Naoko;
                          Miyake, Takahiro; Ohmori, Osamu; Umemura, Ichiro;
                          Steensma, Ruo; Chopiuk, Greg; Jiang, Jiqing; Wan,
                          Yongqin; Ding, Qiang; Zhang, Qiong; Gray, Nathanael
                          Schiander; Karanewsky, Donald
PATENT ASSIGNEE(S):       Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.; IRM
                          LLC
SOURCE:                   PCT Int. Appl., 285 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2005016894         A1    20050224    WO 2004-EP9099          20040813
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
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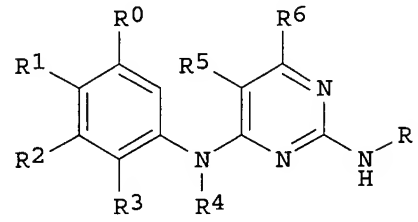
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

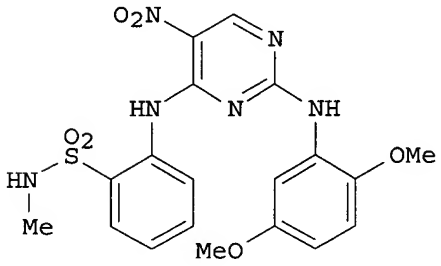
PRIORITY APPLN. INFO.: GB 2003-19227 A 20030815
GB 2003-22370 A 20030924

OTHER SOURCE(S): MARPAT 142:261547

GI



I



II

AB The title compds. I [R = aryl, heteroaryl, cycloalkyl and heterocycloalkyl; R0-R3 = H, alkyl, cycloalkyl, etc.; R4 = H, alkyl; R5, R6 = H, alkyl, alkoxyalkyl, etc.], useful for the manufacture of a medicament for the treatment or prevention of a disease which responds to inhibition of FAK and/or ALK and/or ZAP-70 and/or IGF-IR, were prepared and formulated. E.g., a 2-step synthesis of II, starting from 2,4-dichloro-5-nitropyrimidine and 2-amino-N-methylbenzenesulfonamide, was given. The compds. I have IC50 values in the range of 10 nM to 2 μM in cell-free ZAP-70 kinase assay.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:158646 CAPLUS
DOCUMENT NUMBER: 142:254587
TITLE: Methods for treating or preventing **autoimmune diseases** with **2,4-pyrimidinediamine** compounds
INVENTOR(S): Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati, Somasekhar; Carroll, David; Sylvain, Catherine; Clough, Jeffrey; Keim, Holger
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 276 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016893	A2	20050224	WO 2004-US24716	20040730
WO 2005016893	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 2003-491641P	P	20030730
	US 2003-531598P	P	20031219
	US 2004-572246P	P	20040518

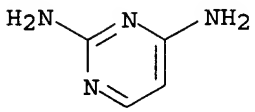
OTHER SOURCE(S): MARPAT 142:254587

AB The invention provides methods for treating or preventing **autoimmune diseases** with **2,4-pyrimidinediamine** compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of **autoimmune diseases** that can be treated or prevented with the compds. include **rheumatoid arthritis** and/or its associated symptoms, **systemic lupus erythematosis** and/or its associated symptoms and **multiple sclerosis** and/or its associated symptoms.

IT **156-81-0D, 2,4-Pyrimidinediamine,** derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyrimidinediamine compds. for treatment or prevention of **autoimmune diseases**)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)



L27 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:120923 CAPLUS

DOCUMENT NUMBER: 142:219300

TITLE: **2,4-Pyrimidinediamines** for use in the treatment or prevention of **autoimmune diseases**

INVENTOR(S): Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati, Somasekhar; Carroll, David; Sylvain, Catherine; Clough, Jeffrey; Keim, Holger

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

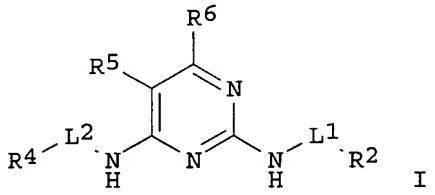
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012294	A1	20050210	WO 2004-US24920	20040730

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2003-491641P P 20030730
US 2003-531598P P 20031219
US 2004-572246P P 20040518

OTHER SOURCE(S): MARPAT 142:219300
GI



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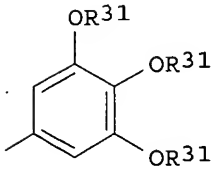

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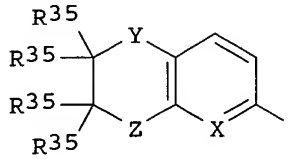


III

AB The present invention provides methods of treating or preventing **autoimmune diseases** with **2,4-pyrimidinediamine** compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl, alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un)substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of **autoimmune diseases** that can be treated or prevented with the compds. I include **rheumatoid arthritis** and/or its associated symptoms, **systemic lupus erythematosus** and/or its associated symptoms and **multiple sclerosis** and/or its associated symptoms. The general procedures for synthesis of compds. I are described. The characterization data for over 500 prepared

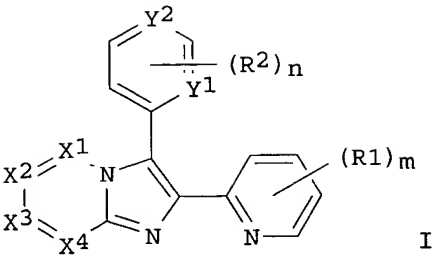
compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5-fluoro-N2-(3,4,5-trimethoxyphenyl)-**2,4-pyrimidinediamine** showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:220155 CAPLUS
DOCUMENT NUMBER: 140:270866
TITLE: Preparation of (pyridinyl)(pyrimidinyl)imidazo[1,2-a]pyridines as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors
INVENTOR(S): Lee, Wen-cherng; Carter, Mary Beth; Sun, Lihong; Chuaqui, Claudio; Singh, Juswinder; Boriack-Sjodin, Paula; Choi, Michael S.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004021989	A2	20040318	WO 2003-US27721		20030905
WO 2004021989	A3	20040923			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2497968	AA	20040318	CA 2003-2497968		20030905
EP 1546112	A2	20050629	EP 2003-752004		20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003014052	A	20050705	BR 2003-14052		20030905
PRIORITY APPLN. INFO.:			US 2002-408812P	P	20020906
			WO 2003-US27721	W	20030905

OTHER SOURCE(S): MARPAT 140:270866
GI



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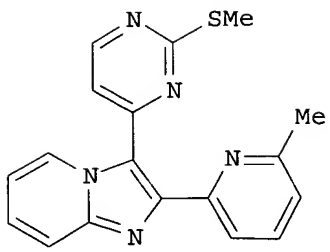
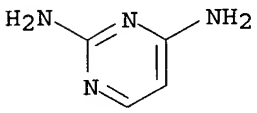


II

AB Title compds. I [wherein X1, X2, X3, X4 = independently CRx or N, only two of them can be N simultaneously; Y1, Y2 = independently CRa or N, at least one of them must be N; R1 = independently alkyl, alkenyl, alkynyl, alkoxy, acyl, urea, cycloalkylsulfanyl, etc.; R2 = independently alkyl, alkenyl, alkynyl, acyl, halo, -N(alkyl)(cycloalkyl), heteroaroyl, etc.; m = 0-4; n = 0-3; Rx, Ra = independently hydrogen, alkyl, alkenyl, hydroxy, guanidino, amidino, cycloalkylcarbonylamino, etc.; and pharmaceutically acceptable salts or N-oxides thereof] were prepared as antagonists against transforming growth factor β (TGFβ) family type I receptors, Alk5 and Alk4. For example, methylation of 2-mercapto-4-methylpyrimidine with MeI, followed by reaction with 6-methylpyridine-2-carboxylic acid Et ester and cyclocondensation with 2-aminopyridine, gave II. I exhibited TGFβ-induced PAI-Luciferase reporter activity with IC50 values of less than 10μM and cytotoxicity with LD25 values greater than 10μM. Thus, I and their pharmaceutical compns. are useful as antagonists for preventing and/or treating numerous diseases, including fibrotic disorders and tumors.

IT **156-81-0**, 2,4-Diaminopyrimidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (pyridinyl)(pyrimidinyl)imidazo[1,2-a]pyridines as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors)

RN 156-81-0 CAPLUS
CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)



L27 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2004:142963 CAPLUS
DOCUMENT NUMBER:	140:199334
TITLE:	Preparation of 2,4-pyrimidinediamines as IgE and/or IgG receptor modulators for treatment of autoimmune diseases
INVENTOR(S):	Singh, Rajinder; Argade, Ankush; Payan, Donald G.; Clough, Jeffrey; Keim, Holger; Sylvain, Catherine; Li, Hui; Bhamidipati, Somasekhar
PATENT ASSIGNEE(S):	Rigel Pharmaceuticals, USA
SOURCE:	PCT Int. Appl., 811 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004014382	A1	20040219	WO 2003-US24087		20030729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2492325	AA	20040219	CA 2003-2492325		20030729
EP 1534286	A1	20050601	EP 2003-784871		20030729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003013059	A	20050705	BR 2003-13059		20030729
US 2005038243	A1	20050217	US 2004-858343		20040601
SE 2005000203	A	20050329	SE 2005-203		20050127
PRIORITY APPLN. INFO.:			US 2002-399673P	P	20020729
			US 2003-443949P	P	20030131
			US 2003-452339P	P	20030306
			US 2003-631029	A	20030729
			US 2002-353267P	P	20020201
			US 2002-353333P	P	20020201
			US 2002-434277P	P	20021217
			US 2003-355543	A1	20030131
			WO 2003-US24087	W	20030729
OTHER SOURCE(S):	MARPAT 140:199334				

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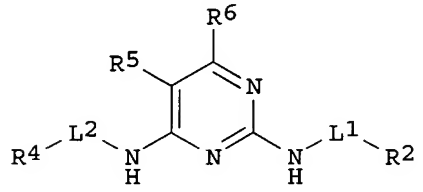

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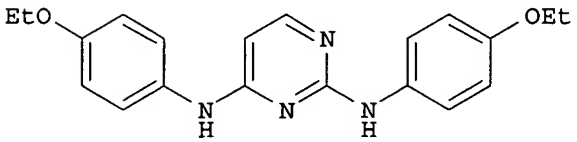


II

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a

linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4-pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM, resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20322 CAPLUS
DOCUMENT NUMBER: 140:87658
TITLE: Peptidomimetic modulators of cell adhesion
INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni, Feng; Chen, Zhigang; Michaud, Stephanie Denise; Wang, Shaomeng; Hu, Zengjian
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 280 pp., Cont.-in-part of U.S. Ser. No. 6,982.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004006011	A1	20040108	US 2003-425557	20030428
US 6031072	A	20000229	US 1997-893534	19970711
US 6326352	B1	20011204	US 2000-507102	20000217
US 2002168761	A1	20021114	US 2001-769145	20010124
US 2002151475	A1	20021017	US 2001-6982	20011204
US 6914044	B2	20050705		

PRIORITY APPLN. INFO.:

US 1996-21612P	P	19960712
US 1997-893534	A1	19970711
US 2000-491078	B2	20000124
US 2000-507102	A1	20000217
US 2001-769145	B2	20010124
US 2001-6982	A2	20011204

OTHER SOURCE(S): MARPAT 140:87658

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such

peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

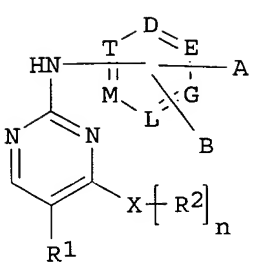
L27 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:737756 CAPLUS
DOCUMENT NUMBER: 139:261319
TITLE: Preparation of 5-bromo-**2,4**-**pyrimidinediamines** and related compounds as cyclin dependent kinase inhibitors
INVENTOR(S): Luecking, Ulrich; Krueger, Martin; Jautelat, Rolf; Prien, Olaf; Siemeister, Gerd; Ernst, Alexander
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076437	A1	20030918	WO 2003-EP1995	20030226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10212100	A1	20031023	DE 2002-10212100	20020311
DE 10255984	A1	20040812	DE 2002-10255984	20021126
EP 1483260	A1	20041208	EP 2003-708151	20030226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004063737	A1	20040401	US 2003-384787	20031027

PRIORITY APPLN. INFO.:

DE 2002-10212100	A	20020311
DE 2002-10255984	A	20021126
US 2002-363878P	P	20020314
US 2002-430053P	P	20021202
WO 2003-EP1995	W	20030226

OTHER SOURCE(S): MARPAT 139:261319
GI



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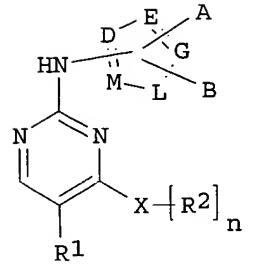
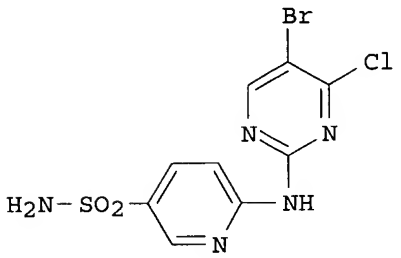


II



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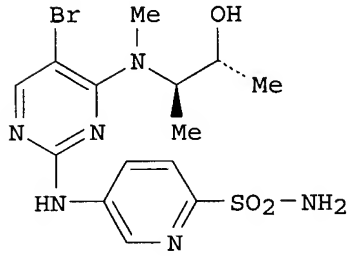


IV

AB Title compds. I and II [D, E, G, L, M, T = C, O, N, S atom whereby at least a heteroatom must be contained in the ring; R1 = H, halo, alkyl, etc.; R2 = H, alkyl, alkenyl, etc.; A, B = H, OH, halo, etc.; n = 0, 1 with provisos] and their pharmaceutically acceptable salts were prepared For example, condensation of chloropyrimidine III, e.g., prepared from 5-bromo-2-chloro-4-hydroxypyrimidine in 2-steps, and threo-3-methylaminobutan-2-ol afforded pyrimidinediamine IV in 75% yield. In CDK2/CycE inhibition studies, 24-examples of compds. I exhibited IC50 values ranging from 6-74 nM. Compds. I are claimed useful as cardiovascular, antiviral, antitumor, etc. agents.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:133036 CAPLUS
DOCUMENT NUMBER: 138:180679
TITLE: SH3 protein domains and their ligands
INVENTOR(S): Booker, Grant William; Pyke, Simon Mathew; Branson, Kim Mathew; Inglis, Steven Robert
PATENT ASSIGNEE(S): Adelaide Research & Innovation Pty Ltd., Australia
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013523	A1	20030220	WO 2002-AU1064	20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2001-6881 A 20010808
OTHER SOURCE(S): MARPAT 138:180679

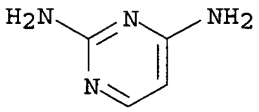
AB The present invention relates generally to mols. capable of interaction with one or more domains within a proteinaceous mol. such as a peptide, polypeptide, protein or a macromol. comprising a proteinaceous mol. More particularly the present invention relates to mols. including ligands which are capable of interacting with, and more particularly, binding to, SH3 protein domains or homologs thereof and even more particularly to mols. including ligands which are capable of binding to SH3 domains having a three-dimensional ligand-binding site comprising a neg. charged residue and a hydrophobic residue linearly separated by at least five amino acid residues. The subject invention is preferably directed to the use of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and derivs., homologs, analogs and mimetics thereof or pharmaceutically acceptable salts thereof which interact with SH3 domains, and more particularly to the binding of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and derivs. analogs and mimetics to SH3 domains as defined above. The present invention contemplates the use of a three dimensional structure of the subject SH3 domain to identify, screen and design amino-substituted and amino-substituted pyridines and aminoquinolines capable of binding to an SH3 domain. The present invention is also useful for the in silico selection of derivs. homologs, analogs and mimetics of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline capable of binding to SH3 domains. The ligands of the present invention are useful in the development of a range of therapeutic and diagnostic agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:91269 CAPLUS
DOCUMENT NUMBER: 139:62596
TITLE: Imidazopyrimidines, potent inhibitors of p38 MAP kinase
AUTHOR(S): Rupert, Kenneth C.; Henry, James R.; Dodd, John H.; Wadsworth, Scott A.; Cavender, Druie E.; Olini, Gilbert C.; Fahmy, Bohumila; Siekierka, John J.
CORPORATE SOURCE: L.L.C., Drug Discovery, Johnson & Johnson Pharmaceutical Research and Development, Raritan, NJ, 08869, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(3), 347-350
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:62596

AB The MAP kinase p38 is implicated in the release of the pro-inflammatory cytokines TNF-α and IL-1β. Inhibition of cytokine release may be a useful treatment for inflammatory conditions such as **rheumatoid arthritis** and Crohn's disease. A novel series of imidazopyrimidines have been discovered that potently inhibit p38 and suppress the production of TNF-α in vivo.

IT **156-81-0, 2,4-Pyrimidinediamine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(imidazopyrimidines, potent inhibitors of p38 MAP kinase)
RN 156-81-0 CAPLUS
CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

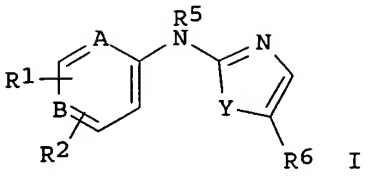


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:449449 CAPLUS
DOCUMENT NUMBER: 137:33318
TITLE: Preparation of pyrimidinylaminothiazoles as tyrosine kinase inhibitors.
INVENTOR(S): Bilodeau, Mark T.; Hartman, George D.; Hoffman, Jacob M., Jr.; Lumma, William C., Jr.; Manley, Peter J.; Rodman, Leonard; Sisko, John T.; Smith, Anthony M.; Tucker, Thomas J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002045652	A2	20020613	WO 2001-US44573	20011130
WO 2002045652	A3	20020822		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002137755	A1	20020926	US 2001-990473	20011121
CA 2429728	AA	20020613	CA 2001-2429728	20011130
AU 2002032441	A5	20020618	AU 2002-32441	20011130
EP 1341540	A2	20030910	EP 2001-991965	20011130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004524282	T2	20040812	JP 2002-547438	20011130
US 2004063720	A1	20040401	US 2003-677687	20031002
PRIORITY APPLN. INFO.:			US 2000-251006P P	20001204
			US 2001-990473 A1	20011121
			WO 2001-US44573 W	20011130

OTHER SOURCE(S): MARPAT 137:33318
GI



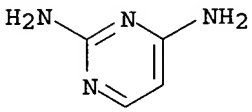
I

AB Title compds. [I; A, B = N, NO; Y = O, S, NR4; R1, R2 = H, perfluoroalkoxy, OH, cyano, halo, (substituted) alkyl(oxy)(carbonyl), aryl(oxy)(carbonyl), heterocyclyl, etc.; R4 = H, aryl, alkyl; R5 = H, SO2Rc, CORc, Rc, CO2Rc; R6 = aryl, cyano, halo, (substituted) alkyl, alkenyl, alkynyl, heterocyclyl, aminocarbonyl; Rc = alkyl, aryl, heterocyclyl], were prepared for treating angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammation, etc. Thus, 4-aminopyrimidine was stirred with NaH in THF; 2-bromo-5-phenylthiazole was added and the mixture was refluxed overnight to give 5-phenylthiazol-2-yl pyrimidin-4-yl amine. I inhibited vascular endothelial growth factor-stimulated mitogenesis of human vascular endothelial cells with IC50 = 0.01-5.0 nM.

IT **156-81-0**, 2,4-Diaminopyrimidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyrimidinylaminothiazoles as tyrosine kinase inhibitors)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)



L27 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:869496 CAPLUS

DOCUMENT NUMBER: 137:363033

TITLE: Peptidomimetic modulators of cell adhesion

INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni, Feng; Chen, Zhigang; Michaud, Stephanie D.; Wang, Shoameng; Hu, Zenjian

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 309 pp., Cont.-in-part of U.S. Ser. No. 491,078.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002168761	A1	20021114	US 2001-769145	20010124
US 2004058864	A1	20040325	US 2003-412701	20030410
US 2004006011	A1	20040108	US 2003-425557	20030428
PRIORITY APPLN. INFO.:			US 2000-491078	A2 20000124
			US 1996-21612P	P 19960712
			US 1997-893534	A1 19970711

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

	US 2000-507102	A1 20000217
	US 2001-769145	B1 20010124
	US 2001-6982	A2 20011204

OTHER SOURCE(S): MARPAT 137:363033

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

L27 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:457043 CAPLUS
DOCUMENT NUMBER: 133:89537
TITLE: Preparation of **2,4-pyrimidinediamine** derivatives as anticancer agents
INVENTOR(S): Bradbury, Robert Hugh; Breault, Gloria Anne; Jewsbury, Philip John; Pease, Janet Elizabeth
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039101	A1	20000706	WO 1999-GB4325	19991220
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2352896	AA	20000706	CA 1999-2352896	19991220
EP 1140860	A1	20011010	EP 1999-962375	19991220
EP 1140860	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9916590	A	20011023	BR 1999-16590	19991220
JP 2002533446	T2	20021008	JP 2000-591012	19991220
AU 763091	B2	20030710	AU 2000-18743	19991220
NZ 512118	A	20030829	NZ 1999-512118	19991220
AT 277020	E	20041015	AT 1999-962375	19991220
ES 2228145	T3	20050401	ES 1999-962375	19991220
ZA 2001004413	A	20020829	ZA 2001-4413	20010529
NO 2001003038	A	20010822	NO 2001-3038	20010619
US 6593326	B1	20030715	US 2001-868602	20010823

PRIORITY APPLN. INFO.:		GB 1998-28511	A 19981224
		WO 1999-GB4325	W 19991220

OTHER SOURCE(S): MARPAT 133:89537
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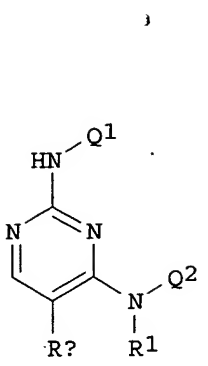

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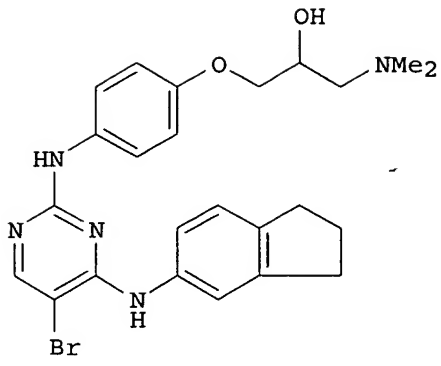

II

AB The present invention relates to the title compds. (I) [wherein R1 = H, (un)substituted alkyl, alkenyl, or alkynyl, benzyl, 2-phenylethyl, phthalimidoalkyl, or cycloalkylalkyl; Rx = halo, OH, NO2, NH2, CN, SH, CO2H, SO2NH2, NHCHO, ureido, etc.; Q1 and Q2 = independently (un)substituted aryl, 5- or 6-membered monocycle, or 9- or 10-membered bicyclic heterocycle], processes for their manufacture, and pharmaceutical compns. containing them. For example, addition of 4-[2-hydroxy-3-(N,N-dimethylamino)propoxy]aniline•HCl in MeOH to 5-bromo-2-chloro-4-(indan-5-ylamino)pyrimidine in BuOH (prepns. given) and heating to 100°C for 18 h gave II (42%). I inhibited the effects of cylin-dependent serine/threonine kinases (CDKs), showing selectivity for CDK2 (no data), CDK4 (IC50 ranging from 0.02 μM to 0.07 μM), and CDK6 (no data). In a tyrosine kinase activity assay using Sf21 cells transfected with plaque-pure FAK recombinant virus, I also inhibited focal adhesion kinase 3 (FAK3) with IC50 ranging from 0.032 μM to 0.07 μM. Typical IC50 values for I when tested for inhibition of cell growth in an Sulforhodamine B (SRB) assay were in the range of 1 mM to 1 nM. Thus, I possess anti-cancer properties, including anti-cell-migration, antiproliferation and/or apoptotic properties. Such properties are expected to be of value in the treatment of disease states associated with aberrant cell cycles and cell proliferation such as cancers (solid tumors and leukemias), fibroproliferative and differentiative disorders, psoriasis, **rheumatoid arthritis**, Kaposi's sarcoma, hemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, **autoimmune diseases**, acute and chronic inflammation, bone diseases, and ocular diseases with retinal vessel proliferation.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 13 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 91081327 EMBASE
DOCUMENT NUMBER: 1991081327
TITLE: Therapy of acute and chronic **multiple sclerosis.**
AUTHOR: Tindall R.S.A.
CORPORATE SOURCE: Department of Neurology, University of Southern California, Los Angeles Veterans Administration Facility, 425 South Hill Street, Los Angeles, CA 90013, United States
SOURCE: Comprehensive Therapy, (1991) Vol. 17, No. 1, pp. 18-25. ISSN: 0098-8243 CODEN: COTHD3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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FILE SEGMENT:        008     Neurology and Neurosurgery
                     026     Immunology, Serology and Transplantation
                     037     Drug Literature Index
LANGUAGE:            English
ENTRY DATE:          Entered STN: 911216
                     Last Updated on STN: 911216
       DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER


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L28        2983 FILE MEDLINE
L29        7931 FILE BIOSIS
L30        2556 FILE EMBASE
L31        9987 FILE CAPLUS

TOTAL FOR ALL FILES
L32       23457 SINGH R?/AU


L33           1 FILE MEDLINE
L34           8 FILE BIOSIS
L35           7 FILE EMBASE
L36          21 FILE CAPLUS

TOTAL FOR ALL FILES
L37          37 ARGADE A?/AU


L38         144 FILE MEDLINE
L39         206 FILE BIOSIS
L40         138 FILE EMBASE
L41         158 FILE CAPLUS

TOTAL FOR ALL FILES
L42         646 PAYAN D?/AU

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L44           1 FILE BIOSIS
L45           0 FILE EMBASE
L46           2 FILE CAPLUS

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L50           0 FILE EMBASE
L51           1 FILE CAPLUS

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PROCESSING COMPLETED FOR L52
L53            2 DUP REM L52 (0 DUPLICATES REMOVED)

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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86
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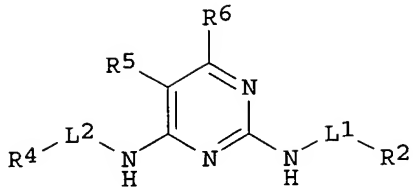
L53 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:610204 CAPLUS
DOCUMENT NUMBER: 139:164801
TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or IgG receptor modulators for treatment of allergic diseases, inflammatory conditions, and tissue destruction
INVENTOR(S): **Singh, Rajinder**; **Argade, Ankush**; **Payan, Donald G.**; Molineaux, Susan; Holland, Sacha J.; Clough, Jeffrey; Keim, Holger; Bhamidipati, Somasekhar; Sylvain, Catherine; Li, Weigun; Rossi, Alexander B.
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 648 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003063794	A2	20030807	WO 2003-US3022		20030131
WO 2003063794	A3	20031204			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2474277	AA	20030807	CA 2003-2474277		20030131
US 2004029902	A1	20040212	US 2003-355543		20030131
EP 1471915	A2	20041103	EP 2003-707654		20030131
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005516046	T2	20050602	JP 2003-563490		20030131
US 2005038243	A1	20050217	US 2004-858343		20040601
PRIORITY APPLN. INFO.:			US 2002-353267P	P	20020201
			US 2002-353333P	P	20020201
			US 2002-399673P	P	20020729
			US 2002-434277P	P	20021217
			US 2003-355543	A1	20030131
			WO 2003-US3022	W	20030131

OTHER SOURCE(S): MARPAT 139:164801
GI



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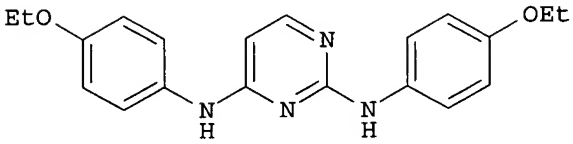

II

AB Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4-pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM, resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. The treatment and prevention of allergic diseases, low grade scarring, diseases associated with tissue destruction, diseases associated with tissue inflammation, inflammation, and scarring are targeted uses (no data).

L53 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:165568 BIOSIS
DOCUMENT NUMBER: PREV200200165568
TITLE: Development and utilization of cultured human mast cells for high throughput small molecule drug discovery.
AUTHOR(S): Rossi, Alexander [Reprint author]; Holland, Sacha [Reprint author]; Woronicz, John [Reprint author]; Quast, Jeff [Reprint author]; **Argade, Ankush**; Sylvain, Catherine; Juencke, Sara; Sula, Caroline; Tombo, Wendy [Reprint author]; Goodrich, Bethany; Pine, Polly; Scheerens, Heleen; Natarajan, Gita; Li, Wenbao; Bennett, Mark [Reprint author]; Daniel, Ruby; Wagner, Gregory; **Singh, Rajinder**; Molineaux, Susan [Reprint author]; **Payan, Donald**
CORPORATE SOURCE: Cell Biology, Rigel Pharmaceuticals, Inc., 240 East Grand Avenue, So. San Francisco, CA, 94080, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 512a-513a. print.
Meeting Info.: 41st Annual Meeting of the American Society

for Cell Biology. Washington DC, USA. December 08-12, 2001.
American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2002
Last Updated on STN: 5 Mar 2002

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L57          70 FILE CAPLUS

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L58         268 KEIM H?/AU


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L62          16 FILE CAPLUS

TOTAL FOR ALL FILES
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L67          10 FILE CAPLUS

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L77           3 FILE CAPLUS

TOTAL FOR ALL FILES
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L79           0 FILE MEDLINE
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L82           3 FILE CAPLUS
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

TOTAL FOR ALL FILES
L83 3 L78 NOT L52

=> d 1-3 ibib abs

L83 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:158646 CAPLUS
DOCUMENT NUMBER: 142:254587
TITLE: Methods for treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compounds
INVENTOR(S): Rajinder, Singh; Ankush, Argade; **Li, Hui**; **Bhamidipati, Somasekhar**; Carroll, David; **Sylvain, Catherine**; Clough, Jeffrey; **Keim, Holger**
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 276 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016893	A2	20050224	WO 2004-US24716	20040730
WO 2005016893	A3	20050609		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 2003-491641P	P	20030730
	US 2003-531598P	P	20031219
	US 2004-572246P	P	20040518

OTHER SOURCE(S): MARPAT 142:254587
AB The invention provides methods for treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosis and/or its associated symptoms and multiple sclerosis and/or its associated symptoms.

L83 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:120923 CAPLUS
DOCUMENT NUMBER: 142:219300
TITLE: 2,4-Pyrimidinediamines for use in the treatment or prevention of autoimmune diseases
INVENTOR(S): Rajinder, Singh; Ankush, Argade; **Li, Hui**; **Bhamidipati, Somasekhar**; Carroll, David; **Sylvain, Catherine**; Clough, Jeffrey; **Keim, Holger**
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012294	A1	20050210	WO 2004-US24920	20040730

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-491641P P 20030730
US 2003-531598P P 20031219
US 2004-572246P P 20040518

OTHER SOURCE(S): MARPAT 142:219300
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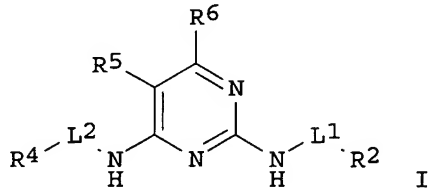

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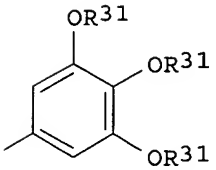

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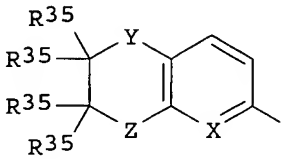

III

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl, alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un)substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. I include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosus and/or its associated symptoms and multiple sclerosis and/or its associated symptoms. The general procedures

for synthesis of compds. I are described. The characterization data for over 500 prepared compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5-fluoro-N2-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:142963 CAPLUS
DOCUMENT NUMBER: 140:199334
TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or IgG receptor modulators for treatment of autoimmune diseases
INVENTOR(S): Singh, Rajinder; Argade, Ankush; Payan, Donald G.; Clough, Jeffrey; **Keim, Holger**; **Sylvain, Catherine**; **Li, Hui**; **Bhamidipati, Somasekhar**
PATENT ASSIGNEE(S): Rigel Pharmaceuticals, USA
SOURCE: PCT Int. Appl., 811 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004014382	A1	20040219	WO 2003-US24087		20030729
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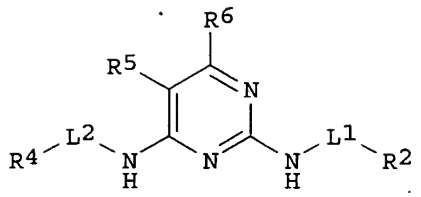
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2492325	AA	20040219	CA 2003-2492325		20030729
EP 1534286	A1	20050601	EP 2003-784871		20030729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003013059	A	20050705	BR 2003-13059		20030729
US 2005038243	A1	20050217	US 2004-858343		20040601
SE 2005000203	A	20050329	SE 2005-203		20050127
PRIORITY APPLN. INFO.:			US 2002-399673P	P	20020729
			US 2003-443949P	P	20030131
			US 2003-452339P	P	20030306
			US 2003-631029	A	20030729
			US 2002-353267P	P	20020201
			US 2002-353333P	P	20020201
			US 2002-434277P	P	20021217
			US 2003-355543	A1	20030131
			WO 2003-US24087	W	20030729

OTHER SOURCE(S): MARPAT 140:199334
GI



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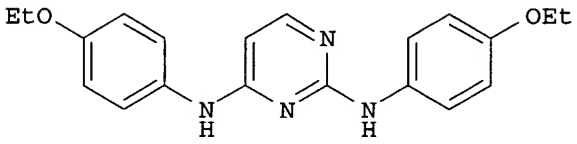

II

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4-pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM, resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his

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FILE 'REGISTRY' ENTERED AT 10:15:38 ON 17 AUG 2005
E "2,4-PYRIMIDINEDIAMINE"/CN 5
L1 1 S E3
E "R 921302"/CN 5
E "R921302"/CN 5
E "R 926891"/CN 5

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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L59             8 FILE MEDLINE
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L61             7 FILE EMBASE
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L63            49 S BHAMIDIPATI S?/AU
L64             8 FILE MEDLINE
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L66            11 FILE EMBASE
L67            10 FILE CAPLUS
     TOTAL FOR ALL FILES
L68            42 S SYLVAIN C?/AU
L69          5342 FILE MEDLINE
L70          6316 FILE BIOSIS
L71          4069 FILE EMBASE
L72         21181 FILE CAPLUS
     TOTAL FOR ALL FILES
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L77             3 FILE CAPLUS
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L80             0 FILE BIOSIS
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L83             3 S L78 NOT L52

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FULL ESTIMATED COST                             138.76     146.93

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CA SUBSCRIBER PRICE                             -11.68     -11.68

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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86